

## STEP THERAPY POLICY

- POLICY:** Antidepressants – Selective Serotonin Reuptake Inhibitor Step Therapy Policy
- Brisdelle<sup>®</sup> (paroxetine mesylate 7.5 mg capsules – Noven Therapeutics, generics)
  - Celexa<sup>®</sup> (citalopram tablets and oral solution – Forest, generics)
  - fluvoxamine tablets (generics)
  - Lexapro<sup>®</sup> (escitalopram tablets and oral solution – Forest, generics)
  - Luvox<sup>®</sup> CR (fluvoxamine extended-release capsules – Jazz, generics)
  - Paxil<sup>®</sup> (paroxetine hydrochloride tablets and oral suspension – GlaxoSmithKline, generics)
  - Paxil CR<sup>®</sup> (paroxetine hydrochloride controlled-release tablets – GlaxoSmithKline, generics)
  - Pexeva<sup>®</sup> (paroxetine mesylate tablets – JDS Pharmaceuticals)
  - Prozac<sup>®</sup> (fluoxetine capsules, tablets, and oral solution – Lilly, generics)
  - Prozac<sup>®</sup> Weekly<sup>™</sup> (fluoxetine delayed-release capsules – Lilly, generics)
  - Sarafem<sup>®</sup> (fluoxetine capsules – generics only)
  - Sarafem<sup>®</sup> (fluoxetine tablets – Warner Chilcott)
  - Trintellix<sup>™</sup> (formerly Brintellix<sup>®</sup>) [vortioxetine tablets – Takeda]
  - Viibryd<sup>®</sup> (vilazodone hydrochloride tablets – Forest)
  - Zoloft<sup>®</sup> (sertraline tablets and oral solution – Pfizer, generics)

**REVIEW DATE:** 02/17/2021

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### OVERVIEW

The selective serotonin reuptake inhibitors (SSRIs) are a pharmacologic class of agents with antidepressant action and efficacy in the treatment of a wide range of mood and anxiety disorders (see Table 1).<sup>1-13</sup> In addition to being an SSRI, Viibryd is also a partial agonist at serotonergic 5-HT<sub>1A</sub> receptors; however, the net result of this action on serotonergic transmission and its role in Viibryd's antidepressant effect are unknown.<sup>11</sup> Similarly, the antidepressant effect of Brintellix is thought to be related to its enhancement of serotonergic activity in the central nervous system (CNS) through inhibition of the reuptake of serotonin.<sup>12</sup> Trintellix (formerly Brintellix) also antagonizes 5-HT<sub>3</sub> receptors and has an agonist effect on 5-HT<sub>1A</sub> receptors; however, the contribution of these activities to the antidepressant effect of Trintellix (formerly Brintellix) has not been established.

**Table 1. FDA-Approved Indications.**<sup>1-13</sup>

Brand (generic)	MDD	OCD	Panic Disorder	Bulimia Nervosa	PTSD	Social Anxiety Disorder	GAD	PMDD	VMS
Brisdelle <sup>®</sup> (paroxetine mesylate 7.5 mg capsules, generics)									X
Celexa <sup>®</sup> (citalopram tablets and oral solution, generics)	X								
Fluvoxamine (generics only)		X <sup>†</sup>							
Lexapro <sup>®</sup> (escitalopram tablets and oral solution, generics)	X <sup>a</sup>						X		
Luvox CR <sup>®</sup> (fluvoxamine extended-release capsules, generics)		X <sup>†</sup>				X			

**Table 1 (continued). FDA-Approved Indications.**<sup>1-13</sup>

Brand (generic)	MDD	OCD	Panic Disorder	Bulimia Nervosa	PTSD	Social Anxiety Disorder	GAD	PMDD	VMS
Paxil <sup>®</sup> (paroxetine HCl tablets and oral suspension, generics)	X	X	X		X	X	X		
Paxil CR <sup>®</sup> (paroxetine HCl controlled-release tablets, generics)	X		X			X		X	
Pexeva <sup>®</sup> (paroxetine mesylate tablets)	X	X	X				X		
Prozac <sup>®</sup> (fluoxetine capsules, tablets, and oral solution, generics)	X <sup>†</sup>	X <sup>†</sup>	X	X					
Prozac <sup>®</sup> Weekly <sup>™</sup> (fluoxetine delayed-release capsules, generics)	X <sup>*</sup>								
Sarafem <sup>®</sup> (fluoxetine capsules and tablets, generics)								X	
Trintellix <sup>™</sup> (formerly Brintellix <sup>®</sup> ) [vortioxetine tablets]	X								
Viibryd <sup>®</sup> (vilazodone tablets)	X								
Zoloft <sup>®</sup> (sertraline tablets and oral suspension, generics)	X	X <sup>†</sup>	X		X	X		X	

MDD – Major Depressive Disorder; OCD – Obsessive compulsive disorder; PTSD – Posttraumatic stress disorder; GAD – Generalized anxiety disorder; PMDD – Premenstrual dysphoric disorder; VMS – Vasomotor symptoms; <sup>†</sup>FDA-approved indication includes children and adolescents; <sup>α</sup>FDA-approved indication includes adolescents 12 to 17 years of age; CR – Controlled release; HCl – Hydrochloride; \* Approved for the prevention of relapse during the continuation treatment phase of depression.

## POLICY STATEMENT

This program has been developed to encourage the use of one Step 1 Product (Standard Criteria) or two Step 1 Products (High Impact Criteria) prior to the use of a Step 2 Product. If the Step Therapy rule is not met for a Step 2 Product at the point of service, coverage will be determined by the Step Therapy criteria below. All approvals are provided for 1 year in duration.

**Automation:** A patient with a history of one Step 1 Product (Standard Criteria) or two Step 1 Products (High Impact Criteria) within the 130-day look-back period is excluded from Step Therapy. Patients > 18 years of age are targeted in this Step Therapy program.

**Step 1:** generic citalopram tablets, generic citalopram oral solution, generic escitalopram tablets, generic escitalopram oral solution, generic fluoxetine immediate-release capsules, generic fluoxetine oral solution, generic fluvoxamine immediate-release tablets, generic paroxetine HCl immediate-release tablets, generic paroxetine HCl oral suspension, generic sertraline tablets, generic sertraline oral solution, generic fluoxetine delayed-release 90 mg capsule

**Step 2:** Lexapro, Paxil, Paxil CR, Pexeva, Prozac, Prozac Weekly, Sarafem, Celexa, Zoloft, Luvox CR, Viibryd, Trintellix (formerly Brintellix), Brisdelle, generic fluoxetine immediate-release tablets, generic paroxetine HCl controlled-release (CR)/extended-release (ER) tablets, generic paroxetine mesylate capsules, generic fluvoxamine extended-release capsules

### **STANDARD CRITERIA**

1. If the patient has tried one Step 1 Product, approve a Step 2 Product.
2. If the patient is currently taking or has taken Pexeva, Viibryd, or Trintellix (formerly Brintellix) at any time in the past and discontinued its use, approve the Product that they have used.
3. If the patient has suicidal ideation, approve Pexeva, Viibryd, or Trintellix (formerly Brintellix).

### **HIGH IMPACT CRITERIA**

1. If the patient has tried two Step 1 Products, approve a Step 2 Product.
2. If the patient is currently taking or has taken Pexeva, Viibryd, or Trintellix (formerly Brintellix) at any time in the past and discontinued its use, approve the Product that they have used.
3. If the patient has suicidal ideation, approve Pexeva, Viibryd, or Trintellix (formerly Brintellix).

### **REFERENCES**

1. Prozac<sup>®</sup> capsules, tablet, oral solution, Prozac<sup>®</sup> Weekly<sup>™</sup> capsules [prescribing information]. Indianapolis, IN: Eli Lilly and Company; April 2020.
2. Paxil<sup>®</sup> tablets and oral suspension [prescribing information]. Weston, FL: Apotex Corp.; February 2021.
3. Zoloft<sup>®</sup> tablets, oral concentrate [prescribing information]. New York, NY: Pfizer Laboratories; December 2017.
4. Celexa<sup>®</sup> tablets and oral solution [prescribing information]. Irvine, CA: Allergan USA, Inc.; January 2019.
5. Paxil CR<sup>®</sup> controlled-release tablets [prescribing information]. Weston, FL: Apotex Corp.; September 2019.
6. Lexapro<sup>®</sup> tablets/oral solution [prescribing information]. Irvine, CA: Allergan USA, Inc.; August 2020.
7. Pexeva<sup>®</sup> paroxetine mesylate tablets [prescribing information]. Roswell, GA: Sebela Pharmaceutical Inc.; December 2020.
8. Fluvoxamine maleate tablets [prescribing information]. Baudette, MN: ANI Pharmaceuticals, Inc.; December 2019.
9. Sarafem<sup>®</sup> tablets [prescribing information]. Irvine, CA: Allergan USA, Inc.; January 2017.
10. Luvox CR<sup>®</sup> extended-release capsules [prescribing information]. Palo Alto, CA: Jazz Pharmaceuticals, Inc.; January 2017.
11. Viibryd<sup>®</sup> tablets [prescribing information]. Madison, NJ: Allergan USA, Inc.; January 2020.
12. Trintellix<sup>™</sup> (formerly Brintellix<sup>®</sup>) tablets [prescribing information]. Deerfield, IL: Takeda Pharmaceuticals America, Inc and Lundbeck; January 2021.
13. Brisdelle<sup>®</sup> capsules [prescribing information]. Roswell, GA: Sebela Pharmaceuticals Inc.; April 2017.